miR-137 forms a regulatory loop with nuclear receptor TLX and LSD1 in neural stem cells.

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Public Summary:
We show here that a brain-enriched small RNA miR-137 has an essential role in controlling embryonic neural stem cell fate. miR-137 inhibits cell proliferation and stimulates neural differentiation of embryonic neural stem cells. Moreover, miR-137 forms a feedback regulatory loop with nuclear receptor TLX and its transcriptional co-repressor LSD1 to control the dynamics between neural stem cell proliferation and differentiation during neural development.

Scientific Abstract:
miR-137 is a brain-enriched microRNA. Its role in neural development remains unknown. Here we show that miR-137 has an essential role in controlling embryonic neural stem cell fate determination. miR-137 negatively regulates cell proliferation and accelerates neural differentiation of embryonic neural stem cells. In addition, we show that the histone lysine-specific demethylase 1 (LSD1), a transcriptional co-repressor of nuclear receptor TLX, is a downstream target of miR-137. In utero electroporation of miR-137 in embryonic mouse brains led to premature differentiation and outward migration of the transfected cells. Introducing a LSD1 expression vector lacking the miR-137 recognition site rescued miR-137-induced precocious differentiation. Furthermore, we demonstrate that TLX, an essential regulator of neural stem cell self-renewal, represses the expression of miR-137 by recruiting LSD1 to the genomic regions of miR-137. Thus, miR-137 forms a feedback regulatory loop with TLX and LSD1 to control the dynamics between neural stem cell proliferation and differentiation during neural development.